Please add new claim 18:

A4

18. (New Claim) The method of claim 1, wherein the neural precursor cells of step (c) are at least 72% of total cell population.

B

REMARKS

The Office action has requested a new oath or declaration and asked for a petition for submission of color drawings. Claim 12 has been objected to, claims 1, 3-11 and 13 under 35 U.S.C. § 112 and all claims are rejected under 35 U.S.C. § 102. Claims 1, 6-7 and 14-17 are rejected under 35 U.S.C. § 103. In light of the amendments above and the arguments below, applicants respectfully request reconsideration.

New Oath/Declaration

Applicant has enclosed a new oath/declaration in compliance with 37 CFR 1.67(a) signed by inventor Su-Chun Zhang.

Drawings

Applicants are preparing three copies of color figures (Fig. 1, Fig. 2 and Fig. 3) and will file a petition under 37 CFR 1.84(a)(2).

Claim Objections

Claim 12 has been cancelled.

§ 112 Rejections

Claim 1 has been amended to provide support for the limitation "the embryoid bodies."

Claims 4 and 13 have been amended to replace "step d" with "step c."

In claim 3, applicant has clarified the phrase "differential enzymatic treatment and adhesion."

§ 102/§ 103 Rejections - In General

Applicant has amended all claims to clarify that the cells are characterized by rosette formation. The rosette formation in the stem cell culture resembles the neural tube structure in an embryo in terms of structural organization and gene expression. Hence, *in vitro* rosette formation is the equivalence of neural tube development in an embryo. Neural tube is the rudiment of the brain and spinal cord. Therefore, rosette formation is the first sign of neural induction from stem cells. That is why the rosette formation is also regarded as "neural rosette" by Lorenz Studer in his comment on Zhang, et al.'s finding (Nature Biotechnology, volume 19, page 1117, see Appendix A).

As neural precursor cells in the neural tube generate all types of specialized neurons and glial cells in the brain and spinal cord, the neural precursor cells in the rosette formation generate a wide spectrum of

neural cell types (Zhang, et al., 2001, Nature Biotechnology, see Appendix A). Therefore, stem cell-derived neural precursor cells that organize in a rosette formation are the most primitive neural cells known to date. They are different from the neural precursor cells that express neural cell adhesion molecule (NCAM, by Carpenter, et al.) as NCAM-expressing cells are at a later stage of development and have a limited differentiation potential. They are also different from the neural precursor cells from the subventricular brain areas as precursor cells in the subventricular zone give rise to only a few specialized neural cell types (Luskin, et al). The rosette formation in stem cells was first discovered by Applicants.

§ 102

Claims 14-17 are rejected under 35 U.S.C. § 102(e) as being anticipated by Luskin (U.S. 6,251,669) as evidenced by Sandberg (U.S. 2002/0028510A1).

Applicants have now amended independent claims 1 and 14 to clarify that the primate neural precursor cells claimed by applicants are characterized by rosette formations. Applicant directs the Examiner to paragraph 0015, for example, for support. Applicants note that the neural precursors described by Luskin do not evince the rosette formation claimed by Applicants. Additionally

applicants note that Luskin, et al. is investigation rodent cells, not the primate cells claimed by Applicants.

Claims 1-2, 4-6 and 10-16 are rejected under 35 U.S.C. § 102 as being anticipated by Carpenter (WO 01/88104). Applicants proffer the same argument as above. Carpenter does not disclose precursor cells wherein the cells are characterized by rosette formation.

Claims 1-17 are rejected under 35 U.S.C. § 102(a) as being anticipated by Su-Chun Zhang, et al. Applicants have enclosed a declaration disclosing that the Zhang, et al. reference is authored by the inventors. Therefore, the reference cannot stand as 102(a) art.

§ 103

Claims 1, 6-7 and 14-17 are rejected under 35 U.S.C. § 103 as being unpatentable over Carpenter, et al. As asserted above, Carpenter, et al. does not disclose neural precursor cells characterized by rosette formation.

No fees are believed necessary to enter this response. However, if any other fees are necessary, please charge Deposit Account 17-0055.

Respectfully submitted,

Su-Chun Zhang, et al.

August 19, 2002

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Su-Chun Zhang, et al.
Serial No.:	09/970,382
Filed:	October 3, 2001
For:	METHOD OF IN VITRO DIFFERENTIATION OF TRANSPLANTABLE NEURAL PRECURSOR CELLS FROM PRIMATE EMBRYONIC STEM CELLS
Group Art Unit:	1636
Examiner:	Q. Nguyen

Commissioner for Patents
Washington, D.C. 20231

MARKED UP COPY OF THE CLAIMS

In the Claims:

Please cancel claims 2 and 12.

Please amend claims 1, 3, 4, 13 and 14 as follows:

1. (Amended) A method of differentiating primate embryonic stem cells into neural precursor cells, comprising the steps of:

(a) obtaining a primate embryonic stem cell culture,

(b) propagating the stem cells, wherein embryoid bodies are formed, and

(c) culturing the embryoid bodies in a medium containing an effective amount of fibroblast growth factor 2, wherein neural precursor[s] cells are generated and wherein the neural precursor cells are characterized by rosette formations.

3. (Amended) The method of claim 1 further comprising the step of isolating the neural precursors by differential enzymatic treatment and adhesion wherein the treatment leads to the preferential detachment of central neuroepithelial islands.

4. (Amended) The method of claim 1 wherein the amount of fibroblast growth factor 2 in the medium of step [(d)] (c) is between 10 and 20 ng/ml.

13. (Amended) The method of claim 1 wherein step [(d)] (c) comprises culturing the embryoid bodies in a medium comprising insulin, transferrin, progesterone, putrescine, sodium selenite and heparin.

14. (Amended) An isolated cell population comprising at least 72% neural precursor cells wherein the cells are characterized by rosette formations.